EPA Comments on Chemical RTK Challenge Submission:

2-Acrylamido-2-methylpropanesulfonic Acid (AMPS® Acid) and Salts

SUMMARY OF EPA COMMENTS

The sponsor, the Lubrizol Corporation, submitted a Test Plan, Category Justification, and Robust Summaries to EPA and posted a Test Plan on the industry HPV Tracking System Web site. EPA posted the submission on the ChemRTK website on September 5, 2000. The proposed information-gathering plan is for a group of two HPV chemicals, 2-Acrylamido-2-methylpropanesulfonic acid (AMPS® acid, CAS No. 15214-89-8) and 2-Acrylamido-2-methylpropanesulfonic acid sodium salt (CAS No. 5165-97-9), and one non-HPV chemical, 2-Acrylamido-2-methylpropanesulfonic acid ammonium salt (CAS No. 58374-69-9).

EPA has reviewed this submission and found that, in general, the test plan and robust summaries were well-organized and easy to follow. The Agency reached the following conclusions:

(1) The Test Plan supports the proposed information gathering on these chemicals as a category. The submission supports the proposed analogy among the two HPV substances and a third non-HPV chemical on the basis of chemical structure and existing data.

(2) Physicochemical and Environmental Fate Data. The sponsor's approach to these endpoints is generally acceptable. However, sponsors need to provide robust summaries for all SIDS endpoints. In this case, the sponsor needs to supply robust summaries for transport/distribution modeling and for estimation of atmospheric oxidation.

(3) Health Endpoints. The sponsor does not propose to conduct any health effects tests, and the robust summaries submitted are adequate for the purpose of the U.S. HPV Challenge Program.

(4) Ecotoxicity Endpoints. The robust summaries for fish and invertebrate studies are adequate for the purpose of the U.S. HPV Challenge Program; however, the algal toxicity summary is inadequate. Without the missing information, EPA cannot evaluate the proposal with respect to this endpoint.

EPA is requesting that the Sponsor advise the Agency within 60 days of any modifications to its submission.

EPA COMMENTS ON AMPS® CATEGORY CHALLENGE SUBMISSION

EPA's comments are organized as follows: Category Definition; Category Justification; Test Plan; Specific Comments on Robust Summaries.

Category Definition

The sponsor postulates that 2-acrylamido-2-methylpropanesulfonic acid and its sodium and ammonium salt are appropriate candidates for review as a chemical category, referred to as the AMPS® category.

Category Justification

EPA believes the presentation adequately supports this category proposal.

The submission presents a case for considering an acid and its sodium and ammonium salts as closely related and for extrapolating data among them. This type of case is relatively simple and often does not require an elaborate justification. However, the sponsor's presentation would have benefited from a brief up-front summary bringing together the information on specific endpoint testing that is scattered throughout the introduction and the endpoint-specific summaries.

The sponsor's principal category justification (section 2.1) lies in the statement, "The members of the AMPS® category are virtually homologous, characterized by a 2- acrylamido-2-methylpropanesulfonic parent anion, distinct only by the corresponding H^+, Na^+ or NH_4^+ counterion (Figure 1)." For the sake of accuracy EPA points out that the members of a homologous series differ in a regular pattern such as the addition of a methylene group, as in ethane, propane, butane, etc. The AMPS® series is not a homologous series in this customary sense; the structures differ only in the counterion associated with the sulfonate anion.

Test Plan

The sponsor's approach to the extrapolation of data among these substances is acceptable.

There are apparent errors in the hydrolysis summary information. Table 2 indicates adequate data only for sodium AMPS®. In contrast, Table 7 indicates adequate data only for ammonium AMPS®. In fact, robust summaries for hydrolysis are presented for both AMPS® acid and sodium AMPS® but not for the ammonium salt. Because many readers may rely heavily on the summary tables, these need to be corrected.

Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient)

The sponsor's approach to the physicochemical endpoint results for the AMPS category is acceptable.

Fate (photodegradation, stability in water, biodegradation, and transport/distribution)

The sponsor's approach to the fate endpoints for AMPS is generally acceptable. For fugacity modeling the sponsor used EQC Level I. EPA recommends using the EQC Level III model from the Canadian Environment Modeling Centre at Trent University. This model can be found at the following Web address: http://www.trentu.ca/academic/aminss/envmodel/.

Health Effects. The sponsor's proposal to address the remaining endpoints by extrapolation from existing data is acceptable.

Environmental Effects. Adequate existing data are available for fish and invertebrates. Deficiencies in the summary for the existing algal study need to be remedied before EPA can evaluate the sponsor's approach to addressing this endpoint (see following section).

Specific Comments on the Robust Summaries

Chemistry

The Robust Summary reports water solubility of ammonium AMPS® to be 761 g/L, i.e., 761 grams of solute per liter of solution. In section 2.1. of the Test Plan, the solubility was restated as "76 gm/100 gm water." Similarly, Table 1A shows a solubility for the AMPS® acid of 10^6 mg/L, while the text in the Test Plan states the solubility as "100 gm/100 gm water." The use of units should be consistent throughout so as to avoid potential confusion.

Fate

The sponsor's robust summary treatment of hydrolysis and biodegradation is acceptable. The sponsor did not include robust summaries for transport/distribution or atmospheric photooxidation. This information is only found in the Test Plan; hence the sponsor needs to provide the summaries.

Health Effects

EPA evaluated 13 health endpoint robust summaries and found one of them to be inadequate for the purposes of the U.S. HPV Challenge Program. EPA acknowledges that all 13 studies were performed under GLP conditions. The inadequate summary of the 1984 Ames test is not considered important because another, adequate summary for a 1991 Ames test with the same test material is sufficient for this endpoint (gene mutation in an *in vitro* bacterial system: 1991 Ames test and *E. coli* test; A.D. Little, Inc., 7/23/91). EPA considers the 1984 summary as supplemental information and the 1991 study as the key study.

The following EPA comments reflect the information in the robust summaries (the full study report may address these comments):

> **CAS#** 15214-89-8 (AMPS® Acid)
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> Mutagenicity data. 1984 Ames Test. According to the summary of a 1984 Ames test (Bioassay Systems Corp, 4/10/84), two separate experiments were conducted. A positive response was seen in the first one which prompted repeating the study to confirm the results. The second study was considered negative. Because specific information (incidence of revertant colonies/dose) was not provided for either study, an independent assessment of the information is not possible.
>
> Mutagenicity data. 1991 Mammalian Cell Cytogenetics Test. Although the study is acceptable

for the Challenge Program, the sponsor needs to report the mitotic indices results in the robust summary for the purpose of providing enough information for an independent assessment of the information.

Mutagenicity data. 1996 Mouse Micronucleus Assay. Although the study is acceptable for the Challenge Program, the sponsor needs to report the PCE/NCE ratio results in the in the robust summary for the purpose of providing enough information for an independent assessment of the information.

Environmental Effects

Robust summaries were submitted for fish and invertebrate studies on each of the three chemicals and for an algal study on CAS# 58374-69-9. The following EPA comments reflect the information in the robust summaries (the full study report may address these comments):

EPA evaluated each robust summary and determined that all six fish and invertebrate studies appear adequate. Some minor deficiencies in the summaries: total organic carbon (TOC) was not reported in the fish and invertebrate summaries; temperature values were not reported in the invertebrate summaries; dissolved oxygen was not reported in the Daphnid robust summary for CAS# 58374-69-9. The sponsor needs to report this information in the summaries.

The robust summary submitted for the algal study on CAS# 58374-69-9 was inadequate, lacking sufficient details to support the reported results. The sponsor needs to provide the number of algal cells/ml counted over time for both control and test concentrations.

Followup Activity

EPA requests that the Sponsor advise the Agency within 60 days of any modifications to its submission.